

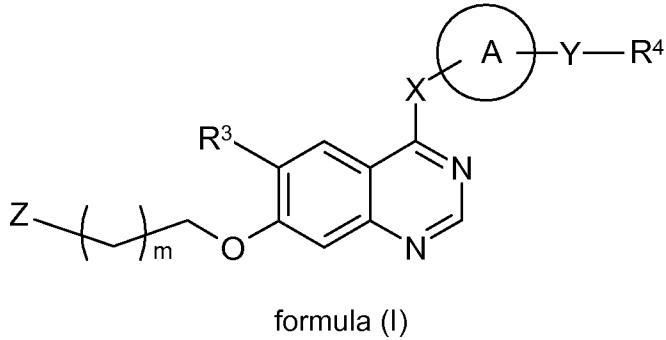
Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

Amendments to the Claims:

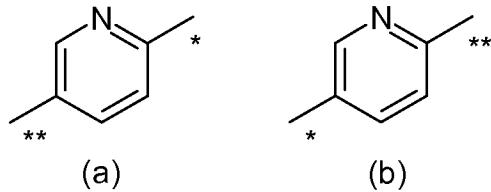
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A compound of formula (I):



wherein **A** is 6-membered heteroaryl containing a nitrogen atom and optionally containing one or two further nitrogen atoms a group of formula (a) or (b):



where * is the point of attachment to the X group of formula (I) and ** is the point of attachment to the Y group of formula (I);

X is O, S, S(O), S(O)₂ or NR¹⁴;

m is 0, 1, 2, 3 or 4;

Y is a group selected from O, NR⁵CO, CONR⁵, CR⁶R⁷CONR⁵ and CR⁶R⁷NR⁵;

Z is a group selected from $-\text{NR}^1\text{R}^2$, phosphonoxy, C_{3-6} cycloalkyl which C_{3-6} cycloalkyl is substituted by phosphonoxy or C_{1-4} alkyl substituted by phosphonoxy, and a 4 to 7 membered ring linked via a carbon atom containing a nitrogen atom and optionally containing a further nitrogen atom, which ring may be saturated, unsaturated or partially saturated which ring is substituted on carbon or nitrogen by phosphonoxy or C_{1-4} alkyl (substituted by phosphonoxy) and which ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C_{1-4} alkyl groups;

R¹ is a group selected from –COR⁸, –CONR⁸R⁹ and C₁₋₆alkyl which C₁₋₆alkyl is substituted by phosphonoxy and optionally further substituted by 1 or 2 halo or methoxy groups;

Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

R² is a group selected from hydrogen, -COR¹⁰, -CONR¹⁰R¹¹ and C₁₋₆alkyl which C₁₋₆alkyl is optionally substituted by 1, 2 or 3 halo or C₁₋₄alkoxy groups, -S(O)_pR¹¹ (where p is 0, 1 or 2) or phosphonoxy, or R² is a group selected from C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

~~or R¹ and R² together with the nitrogen to which they are attached form a 4- to 7-membered ring optionally containing a further nitrogen atom which ring may be saturated, unsaturated or partially saturated which ring is substituted on carbon or nitrogen by a group selected from phosphonoxy and C₁₋₄alkyl substituted by phosphonoxy or NR⁸R⁹, and which ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups;~~

R³ is a group selected from hydrogen, halo, cyano, nitro, C₁₋₆alkoxy, C₁₋₆alkyl, -OR¹², -CHR¹²R¹³, -OC(O)R¹², -C(O)R¹², -NR¹²C(O)R¹³, -C(O)NR¹²R¹³, -NR¹²SO₂R¹³ and -NR¹²R¹³;

R⁴ is hydrogen or a group selected from C₁₋₄alkyl, heteroaryl, heteroarylC₁₋₄alkyl, aryl and arylC₁₋₄alkyl which group is optionally substituted by 1, 2 or 3 substituents selected from halo, methyl, ethyl, cyclopropyl and ethynyl;

R⁵ is a group selected from hydrogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

R⁶ and **R⁷** are independently selected from hydrogen, halo, C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy and C₁₋₄alkoxy;

R⁸ is C₁₋₄alkyl substituted by phosphonoxy and optionally further substituted by 1 or 2 halo or methoxy groups;

R⁹ is selected from hydrogen and C₁₋₄alkyl;

R¹⁰ is selected from hydrogen and C₁₋₄alkyl which C₁₋₄alkyl is optionally substituted by halo, C₁₋₄alkoxy, S(O)_q (where q is 0, 1 or 2) or phosphonoxy;

R¹¹, R¹², R¹³ and R¹⁴ are independently selected from hydrogen, C₁₋₄alkyl and heterocyclyl; or a pharmaceutically acceptable salt thereof.

2. (cancelled)

3. (currently amended) A compound according to claim 2 wherein A is a group of formula (b) ~~or (d)~~ as defined in claim [[2]] 1; or a pharmaceutically acceptable salt thereof.

4. (previously amended) A compound according to claim 1 wherein X is NH; or a pharmaceutically acceptable salt thereof.

Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

5. (canceled)

6. (previously amended) A compound according to claim 1 wherein R¹ is C₁₋₅alkyl substituted by phosphonoxy and R² is hydrogen, C₁₋₅alkyl, C₂₋₄alkynyl or C₃₋₆cycloalkyl; or a pharmaceutically acceptable salt thereof.

7. (cancelled)

8. (previously amended) A compound according to claim 1 wherein R³ is methoxy or hydrogen; or a pharmaceutically acceptable salt thereof.

9. (previously amended) A compound according to claim 1 wherein R⁴ is phenyl or benzyl optionally substituted by 1 or 2 of fluoro or chloro; or a pharmaceutically acceptable salt thereof.

10. (currently amended) A compound selected from:

3-[{(3-{[4-({6-[(3-chlorobenzyl)oxy]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)amino]-3-methylbutyl dihydrogen phosphate;
3-[{(3-{[4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)amino]-3-methylbutyl dihydrogen phosphate;
2-[{(3-{[4-({6-[(3 chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)(ethyl)amino]ethyl dihydrogen phosphate;
~~2-[1-(3-[(4-([6-[(3-chlorobenzoyl)amino]pyridin-3-yl)amino)-6-methoxyquinazolin-7-yl]oxy)propyl]piperidin-2-yl]ethyl dihydrogen phosphate;~~
~~{(2R)-1-(3-[(4-([6-[(3-chlorobenzoyl)amino]pyridin-3-yl)amino)-6-methoxyquinazolin-7-yl]oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;~~
~~2-[1-(3-[(4-([6-[(3-chlorobenzoyl)amino]pyridin-3-yl)amino)-6-methoxyquinazolin-7-yl]oxy)propyl]piperidin-4-yl]ethyl dihydrogen phosphate;~~
2-[ethyl(3-{[4-({6-[(3-fluorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)amino]ethyl dihydrogen phosphate;
2-[{(3-{[4-({6-[(3,4-difluorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)(isopropyl)amino]ethyl dihydrogen phosphate;
~~(3-[(4-([6-[(3-chlorobenzoyl)amino]pyridin-3-yl)amino)-6-methoxyquinazolin-7-yl]oxy)propyl]piperidin-4-yl dihydrogen phosphate;~~

Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

~~4-[{[4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}butyl dihydrogen phosphate;~~
~~2-[{3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](methyl)amino]ethyl dihydrogen phosphate;~~
~~[1-(3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)piperidin-2-yl]methyl dihydrogen phosphate;~~
~~2-[{5-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}pentyl](ethyl)amino]ethyl dihydrogen phosphate;~~
~~4-[{3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](ethyl)amino]butyl dihydrogen phosphate;~~
~~2-[{3-[{4-({6-[(3-fluorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](methyl)amino]ethyl dihydrogen phosphate;~~
~~2-[{3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](isobutyl)amino]ethyl dihydrogen phosphate;~~
~~2-[{3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](cyclopropyl)amino]ethyl dihydrogen phosphate;~~
~~[1-(3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)piperidin-4-yl]methyl dihydrogen phosphate;~~
~~2-[{4-(3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)piperazin-1-yl]ethyl dihydrogen phosphate;~~
~~{(2S)-1-(3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)pyrrolidin-2-yl]methyl dihydrogen phosphate;~~
~~2-[{3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](cyclobutyl)amino]ethyl dihydrogen phosphate;~~
~~2-[{3-[{4-({6-[(3-chlorobenzoyl)amino]pyridin-3-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](prop-2-yn-1-yl)amino]ethyl dihydrogen phosphate;~~
~~2-[{3-[{4-({2-[(3-chloro-4-fluorobenzoyl)amino]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](cyclohexyl)amino]ethyl dihydrogen phosphate;~~
~~2-[{3-[{4-({2-[(3-chloro-4-fluorobenzoyl)amino]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl](ethyl)amino]ethyl dihydrogen phosphate;~~
~~3-[{4-({2-[(3-chlorobenzoyl)amino]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl dihydrogen phosphate;~~
~~1-[3-({4-[(2-[(3-chloro-4-fluorophenyl)amino]methyl)pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)piperidin-4-yl dihydrogen phosphate;~~

Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

3-[(3-{[4-({2-[(3-chloro-4-fluorobenzyl)oxy]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)amino]-3-methylbutyl dihydrogen phosphate;
2-[(3-{[4-({2-[(3-chlorobenzoyl)amino]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy}propyl)(2,2-dimethylpropyl)amino]ethyl dihydrogen phosphate;
~~2-([4-([2-[(3-chloro-4-fluorobenzoyl)amino]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy)methyl)cyclopropylmethyl dihydrogen phosphate;~~ and
~~2-[4-([2-[(3-chloro-4-fluorobenzoyl)amino]pyrimidin-5-yl}amino)-6-methoxyquinazolin-7-yl]oxy)methyl)piperidin-1-yl]ethyl dihydrogen phosphate;~~
or a pharmaceutically acceptable salt thereof.

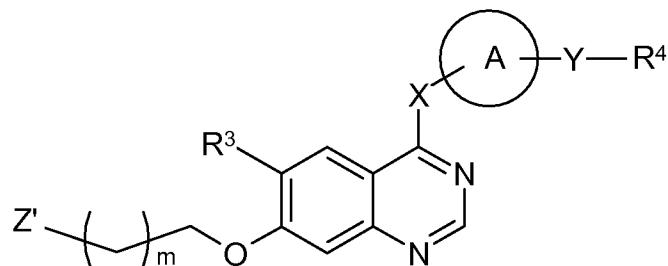
11. (previously amended) A pharmaceutical composition comprising a compound according to claim 1 or a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable diluent or carrier.

12.-15. (cancelled)

16. (withdrawn) A method of treating a human suffering from a disease in which the inhibition of one or more Aurora kinases is beneficial to the treatment, comprising the steps of administering to a person in need thereof a therapeutically effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

17. (withdrawn) A method of treating a human suffering from colorectal, breast, lung, prostate, pancreatic or bladder and renal cancer or leukemias or lymphomas, comprising the steps of administering to a person in need thereof a therapeutically effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

18. (currently amended) A process for the preparation of a compound of formula (I) claim 1 or a pharmaceutically acceptable salt thereof, which process comprises converting a compound of formula (II) into a compound of formula (I) by phosphorylation of an appropriate hydroxy group:



formula (II)

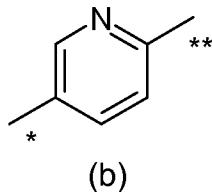
where A, X, m, Y, R³ and R⁴ are as defined for formula (I); and Z' is a group selected from —NR¹R², hydroxy, C₃₋₆cycloalkyl which C₃₋₆cycloalkyl is substituted by hydroxy or C₁₋₄alkyl substituted by hydroxy, and a 4- to 7-membered ring linked via a carbon atom, containing a nitrogen atom and optionally containing a further nitrogen atom, which ring may be saturated, unsaturated or partially saturated and which ring is substituted on carbon or nitrogen by hydroxy or C₁₋₄alkyl substituted by hydroxy and which ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups; R¹ is a group selected from —COR⁸, —CONR⁸R⁹ and C₁₋₆alkyl which C₁₋₆alkyl is substituted by hydroxy and optionally further substituted by 1 or 2 halo or methoxy groups; R² is a group selected from hydrogen, —COR¹⁰, —CONR¹⁰R¹¹ and C₁₋₆alkyl which C₁₋₆alkyl is optionally substituted by 1, 2 or 3 halo or C₁₋₄alkoxy groups, —S(O)_pR¹¹ (where p is 0, 1 or 2) or hydroxy, or R² is a group selected from C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl; or R¹ and R² together with the nitrogen to which they are attached form a 4- to 7-membered ring optionally containing a further nitrogen atom which ring may be saturated, unsaturated or partially saturated and which ring is substituted on carbon or nitrogen by a group selected from hydroxy and C₁₋₄alkyl which C₁₋₄alkyl is substituted by hydroxy or —NR⁸R⁹ and which ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups; and where R⁸ is C₁₋₄alkyl substituted by hydroxy and optionally further substituted by 1 or 2 halo or methoxy groups:

and thereafter if necessary:

- i) converting a compound of the formula (I) into another compound of the formula (I); and/or
- ii) removing any protecting groups; and/or
- iii) forming a pharmaceutically acceptable salt thereof.

19. (withdrawn) The method according to claim 16 wherein Aurora kinase is Aurora-A kinase or Aurora-B kinase.

20. (currently amended) A compound according to claim 1 wherein **A** is a group of formula (b) or (d):



where * is the point of attachment to the X group of formula (I) and ** is the point of attachment to the Y group of formula (I);

X is NH;

m is 0, 1, 2, 3 or 4;

Y is a group selected from O, NR⁵CO, CONR⁵, CR⁶R⁷CONR⁵ and CR⁶R⁷NR⁵;

Z is a group selected from $-\text{NR}^1\text{R}^2$, phosphonoxy, C₃₋₆cycloalkyl which C₃₋₆cycloalkyl is substituted by phosphonoxy or C₁₋₄alkyl substituted by phosphonoxy, and a 4- to 7-membered ring linked via a carbon atom containing a nitrogen atom and optionally containing a further nitrogen atom, which ring may be saturated, unsaturated or partially saturated which ring is substituted on carbon or nitrogen by phosphonoxy or C₁₋₄alkyl (substituted by phosphonoxy) and which ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups;

R¹ is a group selected from $-\text{COR}^8$, $-\text{CONR}^8\text{R}^9$ and C₁₋₆alkyl which C₁₋₆alkyl is substituted by phosphonoxy and optionally further substituted by 1 or 2 halo or methoxy groups;

R² is a group selected from hydrogen, $-\text{COR}^{10}$, $-\text{CONR}^{10}\text{R}^{11}$ and C₁₋₆alkyl which C₁₋₆alkyl is optionally substituted by 1, 2 or 3 halo or C₁₋₄alkoxy groups, $-\text{S(O)}_p\text{R}^{11}$ (where p is 0, 1 or 2) or phosphonoxy, or R² is a group selected from C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

or **R**⁴ and **R**² together with the nitrogen to which they are attached form a 4- to 7-membered ring optionally containing a further nitrogen atom which ring may be saturated, unsaturated or partially saturated which ring is substituted on carbon or nitrogen by a group selected from phosphonoxy and C₁₋₄alkyl substituted by phosphonoxy or $-\text{NR}^8\text{R}^9$, and which ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups;

R³ is a group selected from hydrogen, halo, cyano, nitro, C₁₋₆alkoxy, C₁₋₆alkyl, $-\text{OR}^{12}$, $-\text{CHR}^{12}\text{R}^{13}$, $-\text{OC(O)R}^{12}$, $-\text{C(O)R}^{12}$, $-\text{NR}^{12}\text{C(O)R}^{13}$, $-\text{C(O)NR}^{12}\text{R}^{13}$, $-\text{NR}^{12}\text{SO}_2\text{R}^{13}$ and $-\text{NR}^{12}\text{R}^{13}$;

R⁴ is phenyl or benzyl optionally substituted by 1 or 2 of fluoro or chloro;

R⁵ is a group selected from hydrogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

R⁶ and **R**⁷ are independently selected from hydrogen, halo, C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy and C₁₋₄alkoxy;

R⁸ is C₁₋₄alkyl substituted by phosphonoxy and optionally further substituted by 1 or 2 halo or methoxy groups;

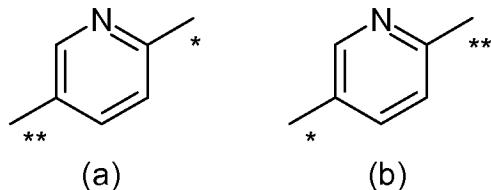
R⁹ is selected from hydrogen and C₁₋₄alkyl;

R¹⁰ is selected from hydrogen and C₁₋₄alkyl which C₁₋₄alkyl is optionally substituted by halo, C₁₋₄alkoxy, S(O)_q (where q is 0, 1 or 2) or phosphonoxy;

R¹¹, **R**¹² and **R**¹³ are independently selected from hydrogen, C₁₋₄alkyl and heterocyclyl; or a pharmaceutically acceptable salt thereof.

21. (Currently amended) A compound according to claim 1, wherein:

A is a group of formula (a), (b), (c) or (d) or (b):



where * is the point of attachment to the X group of formula (I) and ** is the point of attachment to the Y group of formula (I);

X is NH;

m is 0, 1, 2, 3 or 4;

Y is O, NR⁵CO or CR⁶R⁷NR⁵

Z is -NR¹R², phosphonoxy, cyclopropyl which cyclopropyl is substituted by C₁₋₄alkyl substituted by phosphonoxy, and a piperidine or piperazine ring linked via a carbon atom which ring is substituted on carbon or nitrogen by phosphonoxy or C₁₋₄alkyl substituted by phosphonoxy;

R⁴ is C₄₋₅alkyl substituted by phosphonoxy;

R² is a group selected from hydrogen, C₁₋₆alkyl which C₁₋₆alkyl is optionally substituted by 1, 2 or 3 halo or C₁₋₄alkoxy groups, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

R³ is C₁₋₄alkoxy or hydrogen;

R⁴ is phenyl or benzyl optionally substituted by 1 or 2 of fluoro or chloro;

R⁵ is hydrogen or methyl; and

R⁶ and **R**⁷ are independently hydrogen, fluoro, chloro or methyl; or a pharmaceutically acceptable salt thereof.

22. (cancelled)

Application No. 10/539,483
Amendment Dated June 3, 2008
Reply to Office Action of April 3, 2008

23. (previously presented) A pharmaceutical composition comprising a compound according to claim 10 or a pharmaceutically acceptable salt thereof in association with a pharmaceutically acceptable diluent or carrier.